

WO 2004/005923

SEQUENCE LISTING

<110> EXELIXIS, INC.

<120> RABS AS MODIFIERS OF THE p53 PATHWAY AND METHODS OF USE

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<150> US 60/394,992

<151> 2002-07-10

<150> US 60/410,988

<151> 2002-09-16

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&lt;211&gt; 1176

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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 <213> Homo sapiens

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&lt;210&gt; 28

&lt;211&gt; 1608

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 28

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&lt;210&gt; 29

&lt;211&gt; 921

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 29

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&lt;210&gt; 30

&lt;211&gt; 967

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 30

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&lt;211&gt; 899

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 31

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 <212> PRT  
 <213> Homo sapiens

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Phe Ser Asn Gln Tyr Lys Ala Thr Ile Gly Ala Asp Phe Leu Thr Lys  
 35 40 45

Glu Val Met Val Asp Asp Arg Leu Val Thr Met Gln Ile Trp Asp Thr  
 50 55 60

Ala Gly Gln Glu Arg Phe Gln Ser Leu Gly Val Ala Phe Tyr Arg Gly  
 65 70 75 80

Ala Asp Cys Cys Val Leu Val Phe Asp Val Thr Ala Pro Asn Thr Phe  
 85 90 95

Lys Thr Leu Asp Ser Trp Arg Asp Glu Phe Leu Val Gln Ala Ser Pro  
 100 105 110

Arg Asp Pro Glu Asn Phe Pro Phe Val Val Leu Gly Asn Lys Val Asp  
 115 120 125

Leu Glu Asn Arg Gln Val Ala Thr Lys Arg Ala Gln Ala Trp Cys Tyr  
 130 135 140

Ser Lys Asn Asn Ile Pro Tyr Phe Glu Thr Ser Ala Lys Glu Ala Ile  
 145 150 155 160

Asn Val Glu Gln Ala Phe Gln Thr Ile Ala Arg Asn Ala Leu Lys Gln  
 165 170 175

Glu Thr Glu Val Glu Leu Tyr Asn Glu Phe Pro Glu Pro Ile Lys Leu  
 180 185 190

Asp Lys Asn Asp Arg Ala Lys Ala Ser Ala Glu Ser Cys Ser Cys  
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<400> 33

Met Thr Ser Arg Lys Lys Val Leu Leu Lys Val Ile Ile Leu Gly Asp  
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 20 25 30

Phe Ser Asn Gln Tyr Lys Ala Thr Ile Gly Ala Asp Phe Leu Ile Lys  
 35 40 45

Glu Val Met Val Asp Asp Arg Leu Val Thr Met Gln Ile Trp Asp Thr  
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Ala Gly Gln Glu Arg Phe Gln Ser Leu Gly Val Ala Phe Tyr Arg Gly  
 65 70 75 80

Ala Asp Cys Cys Val Leu Val Phe Asp Val Thr Ala Pro Asn Thr Phe  
 85 90 95

Lys Thr Leu Asp Ser Trp Arg Asp Glu Phe Leu Ile Gln Ala Ser Pro  
 100 105 110

Arg Asp Pro Glu Asn Phe Pro Phe Val Val Leu Gly Asn Lys Ile Asp  
 115 120 125

Leu Glu Asn Arg Gln Val Ala Thr Lys Arg Ala Gln Ala Trp Cys Tyr  
 130 135 140

Ser Lys Asn Asn Ile Pro Tyr Phe Glu Thr Ser Ala Lys Glu Ala Ile  
 145 150 155 160

Asn Val Glu Gln Ala Phe Gln Thr Ile Ala Arg Asn Ala Leu Lys Gln  
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Glu Thr Glu Glu Glu Leu Tyr Asn Glu Phe Pro Glu Pro Ile Lys Leu

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185

190

Asp Lys Asn Asp Arg Ala Lys Ala Ser Ala Glu Ser Cys Ser Cys  
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 <400> 34

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 20 25 30

Phe Tyr Glu Glu Tyr Gln Thr Thr Leu Gly Ala Ser Ile Leu Ser Lys  
 35 40 45

Ile Ile Ile Leu Gly Asp Thr Thr Leu Lys Leu Gln Ile Trp Asp Thr  
 50 55 60

Gly Gly Gln Glu Arg Phe Arg Ser Met Val Ser Thr Phe Tyr Lys Gly  
 65 70 75 80

Ser Asp Gly Cys Ile Leu Ala Phe Asp Val Thr Asp Leu Glu Ser Phe  
 85 90 95

Glu Ala Leu Asp Ile Trp Arg Gly Asp Val Leu Ala Lys Ile Val Pro  
 100 105 110

Met Glu Gln Ser Tyr Pro Met Val Leu Leu Gly Asn Lys Ile Asp Leu  
 115 120 125

Ala Asp Arg Lys Val Pro Gln Glu Val Ala Gln Gly Trp Cys Arg Glu  
 130 135 140

Lys Asp Ile Pro Tyr Phe Glu Val Ser Ala Lys Asn Asp Ile Asn Val  
 145 150 155 160

Val Gln Ala Phe Glu Met Leu Ala Ser Arg Ala Leu Ser Arg Tyr Gln  
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Ser Ile Leu Glu Asn His Leu Thr Glu Ser Ile Lys Leu Ser Pro Asp  
 180 185 190

Gln Ser Arg Ser Arg Cys Cys  
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<210> 35  
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<212> PRT  
<213> Homo sapiens

<400> 35

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Gly Val Gly Lys Ser Ser Leu Met Asn Arg Tyr Val Thr Asn Lys Phe  
20 25 30

Asp Thr Gln Leu Phe His Thr Ile Gly Val Glu Phe Leu Asn Lys Asp  
35 40 45

Leu Glu Val Asp Gly His Phe Val Thr Met Gln Ile Trp Asp Thr Ala  
50 55 60

Gly Gln Glu Arg Phe Arg Ser Leu Arg Thr Pro Phe Tyr Arg Gly Ser  
65 70 75 80

Asp Cys Cys Leu Leu Thr Phe Ser Val Asp Asp Ser Gln Ser Phe Gln  
85 90 95

Asn Leu Ser Asn Trp Lys Lys Glu Phe Ile Tyr Tyr Ala Asp Val Lys  
100 105 110

Glu Pro Glu Ser Phe Pro Phe Val Ile Leu Gly Asn Lys Ile Asp Ile  
115 120 125

Ser Glu Arg Gln Val Ser Thr Glu Glu Ala Gln Ala Trp Cys Arg Asp  
130 135 140

Asn Gly Asp Tyr Pro Tyr Phe Glu Thr Ser Ala Lys Asp Ala Thr Asn  
145 150 155 160

Val Ala Ala Ala Phe Glu Glu Ala Val Arg Arg Val Leu Ala Thr Glu  
165 170 175

Asp Arg Ser Asp His Leu Ile Gln Thr Asp Thr Val Asn Leu His Arg  
180 185 190

Lys Pro Lys Pro Ser Ser Ser Cys Cys  
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<400> 36

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Asp Ser Gln Ala Phe His Thr Ile Gly Val Glu Phe Leu Asn Arg Asp  
 35 40 45

Leu Glu Val Asp Gly Arg Phe Val Thr Leu Gln Ile Trp Asp Thr Ala  
 50 55 60

Gly Gln Glu Arg Phe Lys Ser Leu Arg Thr Pro Phe Tyr Arg Gly Ala  
 65 70 75 80

Asp Cys Cys Leu Leu Thr Phe Ser Val Asp Asp Arg Gln Ser Phe Glu  
 85 90 95

Asn Leu Gly Asn Trp Gln Lys Glu Phe Ile Tyr Tyr Ala Asp Val Lys  
 100 105 110

Asp Pro Glu His Phe Pro Phe Val Val Leu Gly Asn Lys Val Asp Lys  
 115 120 125

Glu Asp Arg Gln Val Thr Thr Glu Glu Ala Gln Thr Trp Cys Met Glu  
 130 135 140

Asn Gly Asp Tyr Pro Tyr Leu Glu Thr Ser Ala Lys Asp Asp Thr Asn  
 145 150 155 160

Val Thr Val Ala Phe Glu Glu Ala Val Arg Gln Val Leu Ala Val Glu  
 165 170 175

Glu Gln Leu Glu His Cys Met Leu Gly His Thr Ile Asp Leu Asn Ser  
 180 185 190

Gly Ser Lys Ala Gly Ser Ser Cys Cys  
 195 200

<210> 37  
 <211> 215

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

Met Ala Ser Arg Gly Ala Thr Arg Pro Asn Gly Pro Asn Thr Gly Asn  
 1 5 10 15

Lys Ile Cys Gln Phe Lys Leu Val Leu Leu Gly Glu Ser Ala Val Gly  
 20 25 30

Lys Ser Ser Leu Val Leu Arg Phe Val Lys Gly Gln Phe His Glu Phe  
 35 40 45

Gln Glu Ser Thr Ile Gly Ala Ala Phe Leu Thr Gln Thr Val Cys Leu  
 50 55 60

Asp Asp Thr Thr Val Lys Phe Glu Ile Trp Asp Thr Ala Gly Gln Glu  
 65 70 75 80

Arg Tyr His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ala Gln Ala Ala  
 85 90 95

Ile Val Val Tyr Asp Ile Thr Asn Glu Glu Ser Phe Ala Arg Ala Lys  
 100 105 110

Asn Trp Val Lys Glu Leu Gln Arg Gln Ala Ser Pro Asn Ile Val Ile  
 115 120 125

Ala Leu Ser Gly Asn Lys Ala Asp Leu Ala Asn Lys Arg Ala Val Asp  
 130 135 140

Phe Gln Glu Ala Gln Ser Tyr Ala Asp Asp Asn Ser Leu Leu Phe Met  
 145 150 155 160

Glu Thr Ser Ala Lys Thr Ser Met Asn Val Asn Glu Ile Phe Met Ala  
 165 170 175

Ile Ala Lys Lys Leu Pro Lys Asn Glu Pro Gln Asn Pro Gly Ala Asn  
 180 185 190

Ser Ala Arg Gly Arg Gly Val Asp Leu Thr Glu Pro Thr Gln Pro Thr  
 195 200 205

Arg Asn Gln Cys Cys Ser Asn  
 210 215

&lt;210&gt; 38

<211> 216  
 <212> PRT  
 <213> Homo sapiens

<400> 38

Met Ala Gly Arg Gly Gly Ala Arg Arg Pro Asn Gly Pro Ala Ala Gly  
 1 5 10 15

Asn Lys Ile Cys Gln Phe Lys Leu Val Leu Leu Gly Glu Ser Ala Val  
 20 25 30

Gly Lys Ser Ser Leu Val Leu Arg Phe Val Lys Gly Gln Phe His Glu  
 35 40 45

Tyr Gln Glu Ser Thr Ile Gly Ala Ala Phe Leu Thr Gln Thr Val Cys  
 50 55 60

Leu Asp Asp Thr Thr Val Lys Phe Glu Ile Trp Asp Thr Ala Gly Gln  
 65 70 75 80

Glu Arg Tyr His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ala Gln Ala  
 85 90 95

Ala Ile Val Val Tyr Asp Ile Thr Asn Thr Asp Thr Phe Ala Arg Ala  
 100 105 110

Lys Asn Trp Val Lys Glu Leu Gln Arg Gln Ala Ser Pro Asn Ile Val  
 115 120 125

Ile Ala Leu Ala Gly Asn Lys Ala Asp Leu Ala Ser Lys Arg Ala Val  
 130 135 140

Glu Phe Gln Glu Ala Gln Ala Tyr Ala Asp Asp Asn Ser Leu Leu Phe  
 145 150 155 160

Met Glu Thr Ser Ala Lys Thr Ala Met Asn Val Asn Glu Ile Phe Met  
 165 170 175

Ala Ile Ala Lys Lys Leu Pro Lys Asn Glu Pro Gln Asn Ala Thr Gly  
 180 185 190

Ala Pro Gly Arg Asn Arg Gly Val Asp Leu Gln Glu Asn Asn Pro Ala  
 195 200 205

Ser Arg Ser Gln Cys Cys Ser Asn  
 210 215

<210> 39  
 <211> 215  
 <212> PRT  
 <213> Homo sapiens

<400> 39

Met Thr Ser Arg Ser Thr Ala Arg Pro Asn Gly Gln Pro Gln Ala Ser  
 1 5 10 15

Lys Ile Cys Gln Phe Lys Leu Val Leu Leu Gly Glu Ser Ala Val Gly  
 20 25 30

Lys Ser Ser Leu Val Leu Arg Phe Val Lys Gly Gln Phe His Glu Tyr  
 35 40 45

Gln Glu Ser Thr Ile Gly Ala Ala Phe Leu Thr Gln Ser Val Cys Leu  
 50 55 60

Asp Asp Thr Thr Val Lys Phe Glu Ile Trp Asp Thr Ala Gly Gln Glu  
 65 70 75 80

Arg Tyr His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ala Gln Ala Ala  
 85 90 95

Ile Val Val Tyr Asp Ile Thr Asn Gln Glu Thr Phe Ala Arg Ala Lys  
 100 105 110

Thr Trp Val Lys Glu Leu Gln Arg Gln Ala Ser Pro Ser Ile Val Ile  
 115 120 125

Ala Leu Ala Gly Asn Lys Ala Asp Leu Ala Asn Lys Arg Met Val Glu  
 130 135 140

Tyr Glu Glu Ala Gln Ala Tyr Ala Asp Asp Asn Ser Leu Leu Phe Met  
 145 150 155 160

Glu Thr Ser Ala Lys Thr Ala Met Asn Val Asn Asp Leu Phe Leu Ala  
 165 170 175

Ile Ala Lys Lys Leu Pro Lys Ser Glu Pro Gln Asn Leu Gly Gly Ala  
 180 185 190

Ala Gly Arg Ser Arg Gly Val Asp Leu His Glu Gln Ser Gln Gln Asn  
 195 200 205

Lys Ser Gln Cys Cys Ser Asn  
 210 215

<210> 40  
 <211> 194  
 <212> PRT  
 <213> Homo sapiens

<400> 40

Met Ala Leu Arg Glu Leu Lys Val Cys Leu Leu Gly Asp Thr Gly Val  
 1 5 10 15

Gly Lys Ser Ser Ile Val Trp Arg Phe Val Glu Asp Ser Phe Asp Pro  
 20 25 30

Asn Ile Asn Pro Thr Ile Gly Ala Ser Phe Met Thr Lys Thr Val Gln  
 35 40 45

Tyr Gln Asn Glu Leu His Lys Phe Leu Ile Trp Asp Thr Ala Gly Gln  
 50 55 60

Glu Arg Phe Arg Ala Leu Ala Pro Met Tyr Tyr Arg Gly Ser Ala Ala  
 65 70 75 80

Ala Ile Ile Val Tyr Asp Ile Thr Lys Glu Glu Thr Phe Ser Thr Leu  
 85 90 95

Lys Asn Trp Val Lys Glu Leu Arg Gln His Gly Pro Pro Asn Ile Val  
 100 105 110

Val Ala Ile Ala Gly Asn Lys Cys Asp Leu Ile Asp Val Arg Glu Val  
 115 120 125

Met Glu Arg Asp Ala Lys Asp Tyr Ala Asp Ser Ile His Ala Ile Phe  
 130 135 140

Val Glu Thr Ser Ala Lys Asn Ala Ile Asn Ile Asn Glu Leu Phe Ile  
 145 150 155 160

Glu Ile Ser Arg Arg Ile Pro Ser Thr Asp Ala Asn Leu Pro Ser Gly  
 165 170 175

Gly Lys Gly Phe Lys Leu Arg Arg Gln Pro Ser Glu Pro Lys Arg Ser  
 180 185 190

Cys Cys

<210> 41  
 <211> 212

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 41

Met Ala Gln Ala His Arg Thr Pro Gln Pro Arg Ala Ala Pro Ser Gln  
 1 5 10 15

Pro Arg Val Phe Lys Leu Val Leu Leu Gly Ser Gly Ser Val Gly Lys  
 20 25 30

Ser Ser Leu Ala Leu Arg Tyr Val Lys Asn Asp Phe Lys Ser Ile Leu  
 35 40 45

Pro Thr Val Gly Cys Ala Phe Phe Thr Lys Val Val Asp Val Gly Ala  
 50 55 60

Thr Ser Leu Lys Leu Glu Ile Trp Asp Thr Ala Gly Gln Glu Lys Tyr  
 65 70 75 80

His Ser Val Cys His Leu Tyr Phe Arg Gly Ala Asn Ala Ala Leu Leu  
 85 90 95

Val Tyr Asp Ile Thr Arg Lys Asp Ser Phe Leu Lys Ala Gln Gln Trp  
 100 105 110

Leu Lys Asp Leu Glu Glu Glu Leu His Pro Gly Glu Val Leu Val Met  
 115 120 125

Leu Val Gly Asn Lys Thr Asp Leu Ser Gln Glu Arg Glu Val Thr Phe  
 130 135 140

Gln Glu Gly Lys Glu Phe Ala Asp Ser Gln Lys Leu Leu Phe Met Glu  
 145 150 155 160

Thr Ser Ala Lys Leu Asn His Gln Val Ser Glu Val Phe Asn Thr Val  
 165 170 175

Ala Gln Glu Leu Leu Gln Arg Ser Asp Glu Glu Gly Gln Ala Leu Arg  
 180 185 190

Gly Asp Ala Ala Val Ala Leu Asn Lys Gly Pro Ala Arg Gln Ala Lys  
 195 200 205

Cys Cys Ala His  
 210

&lt;210&gt; 42

&lt;211&gt; 194

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

Met Ala Ile Arg Glu Leu Lys Val Cys Leu Leu Gly Asp Thr Gly Val  
1 5 10 15

Gly Lys Ser Ser Ile Val Cys Arg Phe Val Gln Asp His Phe Asp His  
20 25 30

Asn Ile Ser Pro Thr Ile Gly Ala Ser Phe Met Thr Lys Thr Val Pro  
35 40 45

Cys Gly Asn Glu Leu His Lys Phe Leu Ile Trp Asp Thr Ala Gly Gln  
50 55 60

Glu Arg Phe His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ser Ala Ala  
65 70 75 80

Ala Val Ile Val Tyr Asp Ile Thr Lys Gln Asp Ser Phe Tyr Thr Leu  
85 90 95

Lys Lys Trp Val Lys Glu Leu Lys Glu His Gly Pro Glu Asn Ile Val  
100 105 110

Met Ala Ile Ala Gly Asn Lys Cys Asp Leu Ser Asp Ile Arg Glu Val  
115 120 125

Pro Leu Lys Asp Ala Lys Glu Tyr Ala Glu Ser Ile Gly Ala Ile Val  
130 135 140

Val Glu Thr Ser Ala Lys Asn Ala Ile Asn Ile Glu Glu Leu Phe Gln  
145 150 155 160

Gly Ile Ser Arg Gln Ile Pro Pro Leu Asp Pro His Glu Asn Gly Asn  
165 170 175

Asn Gly Thr Ile Lys Val Glu Lys Pro Thr Met Gln Ala Ser Arg Arg  
180 185 190

Cys Cys